maintaining the data needed, and c including suggestions for reducing	lection of information is estimated to completing and reviewing the collect this burden, to Washington Headqu uld be aware that notwithstanding ar DMB control number.	ion of information. Send comments arters Services, Directorate for Information	regarding this burden estimate mation Operations and Reports	or any other aspect of th , 1215 Jefferson Davis l	is collection of information, Highway, Suite 1204, Arlington	
1. REPORT DATE 01 AUG 2013				3. DATES COVERED		
4. TITLE AND SUBTITLE				5a. CONTRACT NUMBER		
Re: Coagulation and fluid resuscitation by HyperHES in severe				5b. GRANT NUMBER		
hemorrhage. Response to Letter-to-the-Editor.				5c. PROGRAM ELEMENT NUMBER		
6. AUTHOR(S)				5d. PROJECT NUMBER		
Martini W. Z., Dubick M. A.,				5e. TASK NUMBER		
				5f. WORK UNIT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)  United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX				8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)				10. SPONSOR/MONITOR'S ACRONYM(S)		
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)		
12. DISTRIBUTION/AVAILABILITY STATEMENT  Approved for public release, distribution unlimited						
13. SUPPLEMENTARY NOTES						
14. ABSTRACT						
15. SUBJECT TERMS						
16. SECURITY CLASSIFIC	17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF			
a. REPORT unclassified	b. ABSTRACT <b>unclassified</b>	c. THIS PAGE unclassified	UU	of Pages 1	RESPONSIBLE PERSON	

**Report Documentation Page** 

Form Approved OMB No. 0704-0188 more quickly the hypovolemic shock (small-volume resuscitation concept).

More importantly, recent data have suggested that hypertonic saline would modify coagulation less than a colloid only would.<sup>4</sup> In a model of hemorrhagic shock in pigs, resuscitation resulted in less impairment of clot formation when compared with administration of 6% HES or 4% gelatine.<sup>4</sup>

Contrary to isotonic crystalloids and colloids, which play only the ventricular preload, hypertonic saline also improves the other determinants of cardiac output, namely, ventricular afterload and inotropism.<sup>5</sup>

Finally, the volume of fluids needed to restore a good hemodynamics (mean arterial pressure, 65 mm Hg) is significantly different. By extrapolating the data by Martini et al., it would mean an average volume of 8,500 mL of lactated Ringer's solution for a man of medium weight (118 mL/kg). However, fluid resuscitation using HyperHES will start by an injection of 250 mL (recommended dose is 4 mL/kg).<sup>2</sup>

This last point seems not significant in a hospital context but is important in prehospital or war medicine. Indeed, in the setting of combat casualty care, the soldiers have to carry the first aid kit, and we cannot envisage to load them with so much weight.

In the context of trauma combat casualty care, fluid resuscitation by HyperHES, followed by normal saline infusion, seems to be an interesting option for both medical and tactical reasons.

\*The authors declare no conflicts of interest.

Sylvain Vico, MD Clément Dubost, MD Stéphane Mérat, MD

Anesthesiology and Intensive Care Medicine Hôpital d'Instruction des Armées Bégin Saint Mandé, France

## **REFERENCES**

- Martini WZ, Dubick MA, Blackbourne LH. Comparisons of lactated Ringer's and Hextend resuscitation on hemodynamics and coagulation following femur injury and severe hemorrhage in pigs. J Trauma Acute Care Surg. 2013; 74(3):732–740.
- Dubick MA, Atkins JL. Small-volume fluid resuscitation for the far-forward combat environment: current concepts. *J Trauma*. 2003;54: S43–S45.
- Sharma P, Benford B, Karaian JE, Keneally R. Effects of volume and composition of the resuscitative fluids in the treatment of hemorrhagic shock. *J Emerg Trauma Shock*. 2012;5: 309–315.
- Haas T, Fries D, Holz C, Innerhofer P, Streif W, Klingler A, Hanke A, Velik-Salchner C. Less impairment of hemostasis and reduced

- blood loss in pigs after resuscitation from hemorrhagic shock using the small-volume concept with hypertonic saline/hydroxyethyl starch as compared to administration of 4% gelatin or 6% hydroxyethyl starch solution. *Anesth Analg.* 2008;106:1078–1086, table of contents.
- Kramer GC. Hypertonic resuscitation: physiologic mechanisms and recommendations for trauma care. *J Trauma*. 2003;54:S89–S99.

## Re: Coagulation and fluid resuscitation by HyperHES in severe hemorrhage

In Reply.

We sincerely appreciate the interest in and comment from Drs. Vico, Dubost, and Merat regarding our article of "Comparisons of lactated Ringer's and Hextend resuscitation on hemodynamics and coagulation following femur injury and severe hemorrhage in pigs" published in the Journal of Trauma and Acute Care Surgery.

In our article, we reported that Hextend was effective in restoring hemodynamics and acid-base status with one-third volume of lactated Ringer's solution. However, this advantage was associated with undesired effects on coagulation possibly owing to greater and sustained hemodilution from Hextend resuscitation. Vico et al. reported that the French army uses HyperHES (a colloid and 7.5% saline) and suggested that HyperHES has the potential to be more effective in treating hypovolemic shock. We agree with their comments, since the effects on volume expansion have been reported in a large body of literature with 7.5% hypertonic saline as well as hypertonic saline with colloids such as dextran and hydroxyethyl starch. 1-4 However, we are unaware of studies evaluating the effects of HyperHES on coagulation after hemorrhagic shock. With well-documented effects of large molecular weight hydroxyethyl starch on coagulation and the findings of prolonged compromise in coagulation function from Hextend resuscitation in our study and by others in our group,5,6 additional research effort is warranted to determine the effects of HyperHES on hemostasis under trauma and hemorrhagic shock. Perhaps, the lower molecular weight starch of HyperHES may have less effect on coagulation, but this will require confirmation. In addition, only 3% and 5% hypertonic saline solutions are approved by the US Food and Drug Administration, and HyperHES is not an approved product available in United States. Although the US military would like such a product for resuscitation, the military's Tactical Combat Casualty Care Committee could only recommend Hextend as a lower-dose plasma volume expander for far-forward use. Thus, it is unlikely that a recommendation can be made for HyperHES for US combat casualty care in the near future, but we appreciate Dr. Vico and his colleagues bringing this product to our attention.

\*The authors declare no conflicts of interest.

The opinions or assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

The study that this letter refers to has been conducted in compliance with the Animal Welfare Act, the implementing Animal Welfare Regulations, and the principles of the Guide for the Care and Use of Laboratory Animals.

Wenjun Z. Martini, PhD Michael A. Dubick, PhD

US Army Institute of Surgical Research JBSA Fort Sam Houston San Antonio, Texas

## REFERENCES

- Dubick MA, Atkins JL. Small-volume fluid resuscitation for the far-forward combat environment: current concepts. *J Trauma*. 2003; 54(Suppl 5):S43–S45.
- Sharma P, Benford B, Karaian JE, Keneally R. Effects of volume and composition of the resuscitative fluids in the treatment of hemorrhagic shock. *J Emerg Trauma Shock*. 2012; 5(4):309–315.
- Robinson R, Schwendenwein I, Wacek S, Nell B, Mosing M. Plasma volume and electrolyte changes following intravenous infusion of hypertonic hydroxyethyl starch versus mannitol in healthy dogs. Vet J. 2011;190(2):268–272.
- Kerbaul F, Rondelet B, Benas V, Grisoli D, De Waroquier A, Fesler P, Fusai T, Brimioulle S. Hypertonic saline hydroxyethylstarch restores right ventricular-arterial coupling after normovolemic hemodilution in piglets. *Anesthesiology*. 2011;115(1):136–143.
- Sondeen JL, Prince MD, Kheirabadi BS, Wade CE, Polykratis IA, de Guzman R, Dubick MA. Initial resuscitation with plasma and other blood components reduced bleeding compared to hetastarch in anesthetized swine with uncontrolled splenic hemorrhage. *Transfusion*. 2011;51(4):779–792.
- Kheirabadi BS, Crissey JM, Deguzman R, Perez MR, Cox AB, Dubick MA, Holcomb JB. Effects of synthetic versus natural colloid resuscitation on inducing dilutional coagulopathy and increasing hemorrhage in rabbits. *J Trauma*. 2008;64(5):1218–1228; discussion 1228–1229.
- Butler FK Jr., Blackbourne LH. Battlefield trauma care then and now: a decade of Tactical Combat Casualty Care. J Trauma Acute Care Surg. 2012;73(6 Suppl 5):S395–S402.